

CLAIMS

What is claimed is:

1. An isolated polynucleotide that encodes a polypeptide comprising an amino acid sequence selected from the group consisting of:
 - (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 223 (Pro);
 - (b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 226 (Asn);
 - (c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 249 (Trp);
 - (d) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 250 (Lys) to amino acid number 491 (Arg);
 - (e) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 250 (Lys) to 520 (Arg);
 - (f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 491 (Arg);
 - (g) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 21 (Arg) to amino acid number 520 (Arg);
 - (h) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 491 (Arg);
 - (i) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 1 (Met) to amino acid number 520 (Arg);
 - (j) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 163 (Trp);
 - (k) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 211 (Ser); and
 - (l) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 1 (Met) to amino acid number 211 (Ser).

2. An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of:

(a) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 61 to nucleotide 669; ✓

(b) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 61 to 678;

(c) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 61 to nucleotide 747;

(d) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 748 to nucleotide 1473;

(e) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:18 from nucleotide 748 to nucleotide 1560;

(f) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 61 to nucleotide 1473;

(g) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:18 from nucleotide 61 to nucleotide 1560;

(h) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 1 to nucleotide 1473;

(i) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:18 from nucleotide 1 to nucleotide 1560;

(j) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:20 from nucleotide 61 to nucleotide 489;

(k) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:20 from nucleotide 61 to nucleotide 633; and

(l) a polynucleotide comprising a nucleotide sequence as shown in SEQ ID NO:20 from nucleotide 1 to nucleotide 633.

3. An isolated polynucleotide according to claim 1, wherein the polynucleotide encodes a polypeptide that further comprises a transmembrane domain consisting of residues 227 (Trp) to 249 (Trp) of SEQ ID NO:2.

4. An isolated polynucleotide according to claim 1, wherein the polynucleotide encodes a polypeptide that further comprises an intracellular domain consisting of residues 250 (Lys) to 491 (Arg) of SEQ ID NO:2, or 250 (Lys) to 520 (Arg) of SEQ ID NO:19.

5. An isolated polynucleotide according to claim 1, wherein the polypeptide encoded by the polynucleotide has activity as measured by cell proliferation, activation of transcription of a reporter gene, or wherein the polypeptide encoded by the polynucleotide further binds to an antibody,

wherein the antibody is raised to a polypeptide comprising a sequence of amino acids from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 223 (Pro);

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 226 (Asn);

(c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 249 (Trp);

(d) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 250 (Lys) to amino acid number 491 (Arg);

(e) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 250 (Lys) to 520 (Arg);

(f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 491 (Arg);

(g) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 21 (Arg) to amino acid number 520 (Arg);

(h) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 491 (Arg);

(i) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 1 (Met) to amino acid number 520 (Arg);

(j) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 163 (Trp);

(k) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 211 (Ser); and

(l) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 1 (Met) to amino acid number 211 (Ser); and

wherein the binding of the antibody to the isolated polypeptide is measured by a biological or biochemical assay including radioimmunoassay, radioimmuno-precipitation, Western blot, or enzyme-linked immunosorbent assay.

6. An expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA segment encoding a polypeptide from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 223 (Pro);

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 226 (Asn);

(c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 249 (Trp);

(d) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 250 (Lys) to amino acid number 491 (Arg);

(e) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 250 (Lys) to 520 (Arg);

(f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 491 (Arg);

(g) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 21 (Arg) to amino acid number 520 (Arg);

(h) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 491 (Arg);

(i) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 1 (Met) to amino acid number 520 (Arg);

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(j) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 163 (Trp);

(k) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 211 (Ser); and

(l) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 1 (Met) to amino acid number 211 (Ser); and

a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

7. An expression vector according to claim 6, further comprising a secretory signal sequence operably linked to the DNA segment.

8. A cultured cell comprising an expression vector according to claim 7, wherein the cell expresses a polypeptide encoded by the DNA segment.

9. An expression vector according to claim 6, wherein the polypeptide further comprises a transmembrane domain consisting of residues 227 (Trp) to 249 (Trp) of SEQ ID NO:2.

10. An expression vector according to claim 6, wherein the polypeptide further comprises an intracellular domain consisting of residues 250 (Lys) to 491 (Arg) of SEQ ID NO:2 or 250 (Lys) to 520 (Arg) of SEQ ID NO:19.

11. An expression vector according to claim 6, comprising the following operably linked elements:

a transcription promoter;

a DNA segment encoding a polypeptide from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 223 (Pro);

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 226 (Asn);

(c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 249 (Trp);

(d) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 211 (Ser); and

a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

12. A cultured cell into which has been introduced an expression vector according to claim 11, wherein the cell expresses a soluble receptor polypeptide encoded by the DNA segment.

13. A DNA construct encoding a fusion protein, the DNA construct comprising:

a first DNA segment encoding a polypeptide comprising a sequence of amino acid residues selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 20 (Gly);

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 223 (Pro);

(c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 226 (Asn);

(d) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 249 (Trp);

(e) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 250 (Lys) to amino acid number 491 (Arg);

(f) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 250 (Lys) to amino acid number 520 (Arg);

- (g) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 227 (Trp) to amino acid number 249 (Trp);
- (h) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 227 (Trp) to amino acid number 491 (Arg);
- (i) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 227 (Trp) to amino acid number 520 (Arg);
- (j) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 491 (Arg);
- (k) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 21 (Arg) to amino acid number 520 (Arg);
- (l) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 491 (Arg); and
- (m) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 1 (Met) to amino acid number 520 (Arg);
- (n) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 163 (Trp);
- (o) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 211 (Ser); and
- (p) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 1 (Met) to amino acid number 211 (Ser); and
- at least one other DNA segment encoding an additional polypeptide,
wherein the first and other DNA segments are connected in-frame; and
wherein the first and other DNA segments encode the fusion protein.

14. An expression vector comprising the following operably linked elements:

- a transcription promoter;
a DNA construct encoding a fusion protein according to claim 13; and
a transcription terminator,
wherein the promoter is operably linked to the DNA construct, and the DNA construct is operably linked to the transcription terminator.

15. A cultured cell comprising an expression vector according to claim 14, wherein the cell expresses a polypeptide encoded by the DNA construct.

16. A method of producing a fusion protein comprising:
culturing a cell according to claim 15; and
isolating the polypeptide produced by the cell.

17. An isolated polypeptide comprising a sequence of amino acid residues selected from the group consisting of:

- (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 223 (Pro);
- (b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 226 (Asn);
- (c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 249 (Trp);
- (d) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 250 (Lys) to amino acid number 491 (Arg);
- (e) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 250 (Lys) to 520 (Arg);
- (f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 491 (Arg);
- (g) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 21 (Arg) to amino acid number 520 (Arg);
- (h) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 491 (Arg);
- (i) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 1 (Met) to amino acid number 520 (Arg);
- (j) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 163 (Trp);

(k) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 211 (Ser); and

(l) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 1 (Met) to amino acid number 211 (Ser).

18. An isolated polypeptide according to claim 17, wherein the polypeptide consists of a sequence of amino acid residues that is selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 223 (Pro);

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 226 (Asn);

(c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 249 (Trp);

(d) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 250 (Lys) to amino acid number 491 (Arg);

(e) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 250 (Lys) to 520 (Arg);

(f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 491 (Arg);

(g) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 21 (Arg) to amino acid number 520 (Arg);

(h) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 491 (Arg);

(i) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 1 (Met) to amino acid number 520 (Arg);

(j) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 163 (Trp);

(k) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 211 (Ser); and

(l) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 1 (Met) to amino acid number 211 (Ser).

19. An isolated polypeptide according to claim 17, wherein the polypeptide further comprises a transmembrane domain consisting of residues 227 (Trp) to 249 (Trp) of SEQ ID NO:2.

20. An isolated polypeptide according to claim 17, wherein the polypeptide further comprises an intracellular domain consisting of residues 250 (Lys) to amino acid number 491 (Arg) of SEQ ID NO:2, or 250 (Lys) to amino acid number 520 (Arg) of SEQ ID NO:19.

21. An isolated polynucleotide according to claim 17, wherein the polypeptide has activity as measured by cell proliferation, activation of transcription of a reporter gene, or wherein the polypeptide encoded by the polynucleotide further binds to an antibody,

wherein the antibody is raised to a polypeptide comprising a sequence of amino acids from the group consisting of:

- (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 223 (Pro);
- (b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 226 (Asn);
- (c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 249 (Trp);
- (d) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 250 (Lys) to amino acid number 491 (Arg);
- (e) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 250 (Lys) to 520 (Arg);
- (f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 491 (Arg);
- (g) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 21 (Arg) to amino acid number 520 (Arg);

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(h) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 491 (Arg);

(i) the amino acid sequence as shown in SEQ ID NO:19 from amino acid number 1 (Met) to amino acid number 520 (Arg);

(j) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 163 (Trp);

(k) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 211 (Ser); and

(l) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 1 (Met) to amino acid number 211 (Ser); and

wherein the binding of the antibody to the isolated polypeptide is measured by a biological or biochemical assay including radioimmunoassay, radioimmuno-precipitation, Western blot, or enzyme-linked immunosorbent assay.

22. A method of producing a polypeptide comprising:
culturing a cell according to claim 8; and
isolating the polypeptide produced by the cell.

23. An isolated polypeptide comprising an amino acid segment selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 226 (Asn);

(b) the amino acid sequence as shown in SEQ ID NO:4;

(c) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 211 (Ser); and

(c) sequences that are at least 90% identical to (a), (b) or (c),

wherein the polypeptide is substantially free of transmembrane and intracellular domains ordinarily associated with hematopoietic receptors.

24. A method of producing a polypeptide comprising:
culturing a cell according to claim 12; and

isolating the polypeptide produced by the cell.

25. A method of producing an antibody to a polypeptide comprising:
inoculating an animal with a polypeptide selected from the group consisting
of:

(a) a polypeptide consisting of 50 to 471 amino acids, wherein the
polypeptide comprises a contiguous sequence of amino acids in SEQ ID NO:2 from amino
acid number 21 (Arg), to amino acid number 491 (Arg);

(b) a polypeptide consisting of 50 to 500 amino acids, wherein the
polypeptide comprises a contiguous sequence of amino acids in SEQ ID NO:19 from amino
acid number 21 (Arg), to amino acid number 520 (Arg);

(c) a polypeptide consisting of 50 to 191 amino acids, wherein the
polypeptide comprises a contiguous sequence of amino acids in SEQ ID NO:21 from amino
acid number 21 (Arg), to amino acid number 211 (Ser);

(d) a polypeptide according to claim 18;

(e) a polypeptide comprising amino acid number 21 (Arg) to 119 (Tyr) of
SEQ ID NO:2;

(f) a polypeptide comprising amino acid number 125 (Pro) to 223 (Pro) of
SEQ ID NO:2;

(g) a polypeptide comprising a hydrophilic peptide of SEQ ID NO:2 as
predicted from a hydrophobicity plot using a Hopp/Woods hydrophilicity profile based on a
sliding six-residue window, with buried G, S, and T residues and exposed H, Y, and W
residues ignored; and

wherein the polypeptide elicits an immune response in the animal to produce
the antibody; and

isolating the antibody from the animal.

26. An antibody produced by the method of claim 25, which specifically
binds to a polypeptide of SEQ ID NO:2, SEQ ID NO:19 or SEQ ID NO:21.

27. The antibody of claim 26, wherein the antibody is a monoclonal antibody.

28. An antibody that specifically binds to a polypeptide of claim 17.

29. An antibody that specifically binds to a polypeptide of claim 18.

30. A method of detecting, in a test sample, the presence of a modulator of the activity of a cytokine receptor protein comprising:

culturing a cell into which has been introduced an expression vector according to claim 6, wherein the cell expresses the protein encoded by the DNA segment in the presence and absence of a test sample; and

comparing levels of activity of the protein in the presence and absence of a test sample, by a biological or biochemical assay; and

determining from the comparison, the presence of modulator the cytokine receptor protein activity in the test sample.

31. A method for detecting a cytokine receptor ligand within a test sample, comprising:

contacting a test sample with a cytokine receptor polypeptide comprising an amino acid sequence from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:4;

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 21 (Arg) to amino acid number 226 (Asn); and

(c) the amino acid sequence as shown in SEQ ID NO:21 from amino acid number 21 (Arg) to amino acid number 211 (Ser); and

detecting the binding of the cytokine receptor polypeptide to a ligand in the sample.

32. A method for detecting a cytokine receptor ligand according to claim 31, wherein the cytokine receptor polypeptide is membrane bound within a cultured cell, and the detecting step comprises measuring a biological response in the cultured cell.

33. A method for detecting a cytokine receptor ligand according to claim 32, wherein the biological response is cell proliferation or activation of transcription of a reporter gene.

34. A method for detecting a genetic abnormality in a patient, comprising:
obtaining a genetic sample from a patient;
producing a first reaction product by incubating the genetic sample with a polynucleotide comprising at least 14 contiguous nucleotides of SEQ ID NO:1 or the complement of SEQ ID NO:1, under conditions wherein said polynucleotide will hybridize to complementary polynucleotide sequence;
visualizing the first reaction product; and
comparing said first reaction product to a control reaction product from a wild type patient, wherein a difference between said first reaction product and said control reaction product is indicative of a genetic abnormality in the patient.

35. A method for detecting a cancer in a patient, comprising:
obtaining a tissue or biological sample from a patient;
incubating the tissue or biological sample with an antibody of claim 29 under conditions wherein the antibody binds to its complementary polypeptide in the tissue or biological sample;
visualizing the antibody bound in the tissue or biological sample; and
comparing levels of antibody bound in the tissue or biological sample from the patient to a normal control tissue or biological sample,
wherein an increase in the level of antibody bound to the patient tissue or biological sample relative to the normal control tissue or biological sample is indicative of a cancer in the patient.

36. A method for detecting a cancer in a patient, comprising:
obtaining a tissue or biological sample from a patient;
labeling a polynucleotide comprising at least 14 contiguous nucleotides of
SEQ ID NO:1, SEQ ID NO:18 or SEQ ID NO:20 or the complement of SEQ ID NO:1, SEQ
ID NO:18 or SEQ ID NO:20;
incubating the tissue or biological sample with under conditions wherein the
polynucleotide will hybridize to complementary polynucleotide sequence;
visualizing the labeled polynucleotide in the tissue or biological sample; and
comparing the level of labeled polynucleotide hybridization in the tissue or
biological sample from the patient to a normal control tissue or biological sample,
wherein an increase in the labeled polynucleotide hybridization to the patient
tissue or biological sample relative to the normal control tissue or biological sample is
indicative of a cancer in the patient.

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